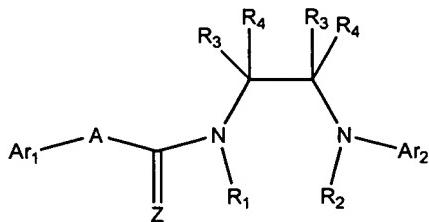


Claims

What is claimed is:

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof,

wherein:

A is absent or is selected from the group consisting of O , S , NR_A , $\text{CR}_\text{B}\text{R}_\text{B}'$, $\text{NR}_\text{A}\text{CR}_\text{B}\text{R}_\text{B}'$, $\text{CR}_\text{B}\text{R}_\text{B}'\text{NR}_\text{A}$, $-\text{CR}_\text{A}=\text{CR}_\text{B}-$, and C_3H_4 ; where R_A , R_B , and R_B' are independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R_1 and R_2 independently represent hydrogen or alkyl;

R_3 and R_4 are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; $-\text{COOH}$; $-\text{CHO}$, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-\text{S}(\text{O})_\text{n}\text{NHalkyl}$; optionally substituted $-\text{S}(\text{O})_\text{n}\text{N(alkyl)(alkyl)}$; optionally substituted $-\text{NHC}(=\text{O})\text{alkyl}$;

optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; or optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

R_3 and R_4 not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S; and

Ar_1 and Ar_2 are the same or different and independently represent optionally substituted cycloalkyl; an optionally substituted heterocycloalkyl ring of from 5 to 8 atoms, which heterocycloalkyl ring contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; or optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S, and

n is independently chosen at each occurrence from 0, 1, and 2.

2. A compound or salt according to Claim 1, wherein:

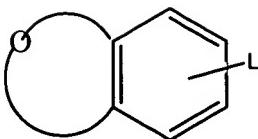
R_3 and R_4 are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6 , alkenyl substituted with 0-2 R_6 ; alkynyl substituted with 0-2 R_6 ; alkoxy substituted with 0-2 R_6 , $-NH(alkyl)$ substituted with 0-2 R_6 , $-N(alkyl)(alkyl)$ where each alkyl is independently substituted with 0-2 R_6 , $-XR_7$, and Y;

or any two

R_3 and R_4 not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R_6 , a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6 , or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar_1 and Ar_2 may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5 ; or

Ar_1 and Ar_2 may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R₅ is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R₆, alkenyl substituted with 0-2 R₆, alkynyl substituted with 0-2 R₆, alkoxy substituted with 0-2 R₆, -NH(alkyl) substituted with 0-2 R₆, -N(alkyl)(alkyl) where each alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -NH(alkyl), -N(alkyl)(alkyl), -S(O)_n(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl₁)(alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups

consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y'; Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

3. A compound or salt according to Claim 1, wherein:

R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen and C₁₋₆alkyl;

R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted

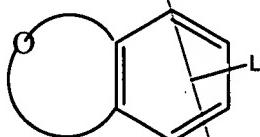
with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

or any two

R₃ and R₄ not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar₁ and Ar₂ may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R₅; or

Ar₁ and Ar₂ may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the

bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R₅ is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

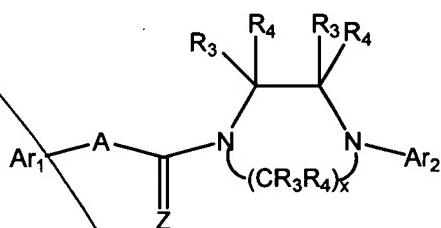
X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy,

~~-O(C₁₋₄alkyl), -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl),
-NHC(O)(C₁₋₄alkyl), -N(C₁₋₄alkyl)C(O)(C₁₋₄alkyl), -NHS(O)_n(C₁₋₄alkyl),
-S(O)_n(C₁₋₄alkyl), -S(O)_nNH(C₁₋₄alkyl),
-S(O)_nN(C₁₋₄alkyl₃)(C₁₋₄alkyl₄) where C₁₋₄alkyl₃ and C₁₋₄alkyl₄
may be joined to form a heterocycloalkyl ring consisting of
from 5 to 8 ring atoms and containing 1, 2, or 3
heteroatoms selected from N, O, and S, and Y';
Y and Y' are independently selected at each occurrence from 3-
to 8-membered carbocyclic or heterocyclic groups which are
saturated, unsaturated, or aromatic, which may be further
substituted with one or more substituents independently
selected from halogen, oxo, hydroxy, amino, nitro, cyano,
C₁₋₄alkyl, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy,
mono- or di(C₁₋₄)alkylamino, and C₁₋₄alkylthio;
wherein said 3- to 8-membered heterocyclic groups contain
one or more heteroatom(s) independently selected from N, O,
and S; and~~

~~n is independently chosen at each occurrence from 0, 1, and 2.~~

4. A compound of the formula:



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or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S,
NR_A, CR_BR_{B'}, NR_ACR_BR_{B'},
CR_BR_{B'}NR_A, -CR_A=CR_B-, and C₃H₄; where R_A, R_B, and R_{B'} are

independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R₃ and R₄ are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -S(O)_nNHalkyl; optionally substituted -S(O)_nN(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted -NHS(O)_nalkyl; optionally substituted -NS(O)_n(alkyl)(alkyl); optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

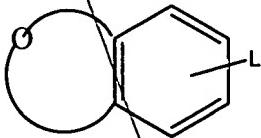
R₃ and R₄ not attached to the same carbon may be joined to form an optionally substituted aryl ring, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted,

or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

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Ar₁ and Ar₂ may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R₅; or

Ar₁ and Ar₂ may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R₅ is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl)

~~6~~alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂- , -CHR₈- , -O- , -S(O)_n- , -NH- , -NR₈- , -C(=O)- , -C(=O)O- , -C(=O)NH- , -C(=O)NR₈- , -S(O)_nNH- , -S(O)_nNR₈- , NHC(=O)- , -NR₈C(=O)- , -NHS(O)_n- , and -NR₈S(O)_n- ;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further

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substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;

n is independently chosen at each occurrence from 0, 1, and 2; and

x is 1 or 3.

5. A compound or salt according to Claim 4, wherein:

~~R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or C₁₋₆alkyl;~~

~~R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆,~~

~~-XR₇, and Y;~~

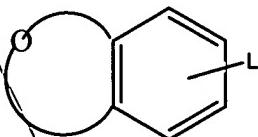
~~or any two~~

~~R₃ and R₄ not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms selected from N, O, and S;~~

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Ar_1 and Ar_2 may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thieryl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5 ; or

Ar_1 and Ar_2 may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R_5 , where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl substituted with 0-2 R_6 , C_{2-6} alkenyl substituted with 0-2 R_6 , C_{2-6} alkynyl substituted with 0-2 R_6 , C_{1-6} alkoxy substituted with 0-2 R_6 , $-\text{NH}(\text{C}_{1-6}\text{alkyl})$ substituted with 0-2 R_6 , $-\text{N}(\text{C}_{1-6}\text{alkyl})(\text{C}_{1-6}\text{alkyl})$ where each C_{1-6} alkyl is independently substituted with 0-2 R_6 , $-\text{XR}_7$, and Y ;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4} alkyl, C_{1-4} alkoxy,

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-NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(C₁₋₄alkyl), -N(C₁₋₄alkyl)C(O)(C₁₋₄alkyl), -NHS(O)_n(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), -S(O)_nNH(C₁₋₄alkyl), -S(O)_nN(C₁₋₄alkyl₃)(C₁₋₄alkyl₄) where C₁₋₄alkyl₃ and C₁₋₄alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano,

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~~C₁₋₄alkyl, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, mono- or di(C₁₋₄)alkylamino, and C₁₋₄alkylthio;~~
wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;

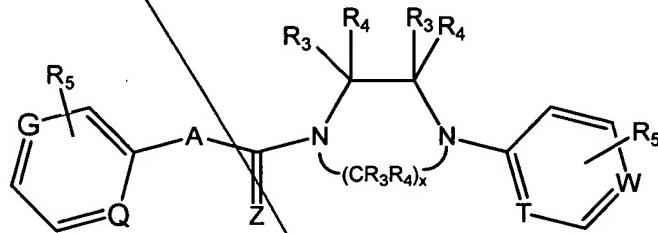
n is independently chosen at each occurrence from 0, 1, and 2;
and

x is 1 or 3.

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6. A compound or salt according to Claim 4, wherein Z is oxygen.

7. A compound or salt according to Claim 4 of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and represent N, CH, or CR₅;

R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or C₁₋₆alkyl;

Z is oxygen or sulfur;

R₃ and R₄ are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally

substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

R₃ and R₄ not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R₅ represents 0 to 3 substituents on each of the aryl rings on which it occurs and is independently chosen at each occurrence from the group consisting of halogen, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl

substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y; R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -NH(alkyl), -N(alkyl)(alkyl), -S(O)_n(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl₁)(alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

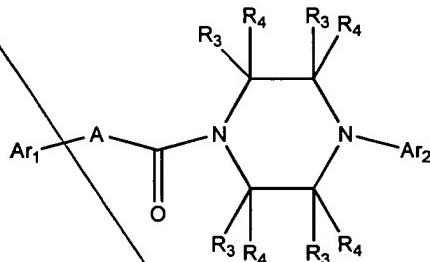
R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

~~Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;~~
~~wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S;~~

n is independently chosen at each occurrence from 0, 1, and 2;
and

x is 1 or 3.

8. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A , $\text{CR}_B\text{R}_B'$, $\text{NR}_A\text{CR}_B\text{R}_B'$, $\text{CR}_B\text{R}_B'\text{NR}_A$, $-\text{CR}_A=\text{CR}_B-$, and C_3H_4 ; where R_A , R_B , and R_B' are independently selected at each occurrence from hydrogen or alkyl;

R_3 and R_4 are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; $-\text{COOH}$; $-\text{CHO}$, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally

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substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

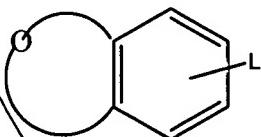
R_3 and R_4 not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar_1 and Ar_2 may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thieryl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl,

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isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl; wherein Ar₁ is optionally mono-, di-, or trisubstituted with R₅, and Ar₂ is optionally mono-, di-, or trisubstituted with R₉; or

Ar₁ and Ar₂ may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R₅ is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R₆, alkenyl substituted with 0-2 R₆, alkynyl substituted with 0-2 R₆, alkoxy substituted with 0-2 R₆, -NH(alkyl) substituted with 0-2 R₆, -N(alkyl)(alkyl) where each alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₉ is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R₆, alkenyl substituted with 0-2 R₆, alkynyl substituted with 0-2 R₆, alkoxy substituted with 0-2 R₆, -NH(alkyl) substituted with 0-2 R₆, -N(alkyl)(alkyl)

where each alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -NH(alkyl), -N(alkyl)(alkyl), -S(O)_n(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl₁)(alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂- , -CHR₈- , -O- , -S(O)_n- , -NH- , -NR₈- , -C(=O)- , -C(=O)O- , -C(=O)NH- , -C(=O)NR₈- , -S(O)_nNH- , -S(O)_nNR₈- , NHC(=O)- , -NR₈C(=O)- , -NHS(O)_n- , and -NR₈S(O)_n- ;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y' ;

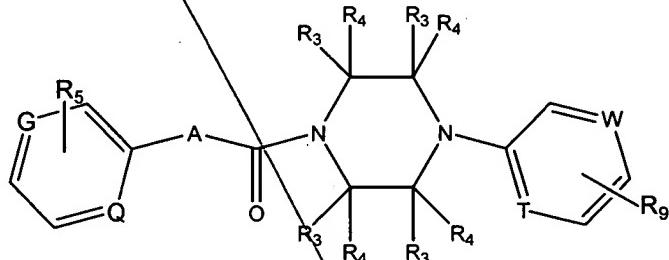
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further

substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

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n is independently chosen at each occurrence from 0, 1, and 2.

9. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and are selected from the group consisting of N, CH, and CR₅, wherein T or W or both is N;

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B- , and C₃H₄; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or alkyl;

Z is oxygen or sulfur;

R₃ and R₄ are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted C₁₋₆alkyl; optionally substituted C₂₋₆alkenyl; optionally substituted C₂₋₆alkynyl; optionally substituted C₁₋₆alkoxy; optionally

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substituted mono or di(C₁₋₆)alkylamino; optionally substituted C₁₋₆alkylthio; optionally substituted C₁₋₆alkyl ketone; optionally substituted C₁₋₆alkylester; optionally substituted C₁₋₆alkylsulfinyl; optionally substituted C₁₋₆alkylsulfonyl; optionally substituted mono- or di(C₁₋₆)alkylcarboxamide; optionally substituted -S(O)_nNH C₁₋₆alkyl; optionally substituted -S(O)_nN(C₁₋₆alkyl) (C₁₋₆alkyl); optionally substituted -NC(=O) (C₁₋₆alkyl) (C₁₋₆alkyl); optionally substituted -NHS(O)_nC₁₋₆alkyl; optionally substituted -NS(O)_n(C₁₋₆alkyl) (C₁₋₆alkyl); optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

R₃ and R₄ not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R₅ represents 1 to 3 substituents and is independently selected at each occurrence from the group consisting of cyano, hydroxy, amino, C₃₋₆ alkyl substituted with 0-2 R₆, C₂₋₆

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alkenyl substituted with 0-2 R₆, C₂₋₆ alkynyl substituted with 0-2 R₆, C₃₋₆ alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₉ represents 0 to 3 substituents and is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more

substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}\text{alkyl})$, $-\text{NH}(C_{1-4}\text{alkyl})$, $-\text{N}(C_{1-4}\text{alkyl})(C_{1-4}\text{alkyl})$, $-\text{NHC(O)}(C_{1-4}\text{alkyl})$, $-\text{N}(C_{1-4}\text{alkyl})\text{C(O)}(C_{1-4}\text{alkyl})$, $-\text{NHS(O)}_n(C_{1-4}\text{alkyl})$, $-\text{S(O)}_n(C_{1-4}\text{alkyl})$, $-\text{S(O)}_n\text{NH}(C_{1-4}\text{alkyl})$, $-\text{S(O)}_n\text{N}(C_{1-4}\text{alkyl}_3)(C_{1-4}\text{alkyl}_4)$ where $C_{1-4}\text{alkyl}_3$ and $C_{1-4}\text{alkyl}_4$ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y'; and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, $C_{1-4}\text{alkyl}$, $C_{1-4}\text{alkoxy}$, $\text{halo}(C_{1-4})\text{alkyl}$, $\text{halo}(C_{1-4})\text{alkoxy}$, mono- or di(C_{1-4})alkylamino, and $C_{1-4}\text{alkylthio}$; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and independently chosen at each occurrence from 0, 1, and 2.

10. A compound according to Claim 9, which is 4-(3-Chloro-2-pyridinyl)-N-[4(isopropyl)phenyl]-2-methylthio-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

11. A compound according to Claim 9, wherein R₃ and R₄ are independently selected at each occurrence from the group consisting of hydrogen and C₁₋₆ alkyl.

12. A compound according to Claim 11, wherein G and Q are selected from the group consisting of CH and CR₅.

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13. A compound according to Claim 11, wherein G , Q, and W are independently selected at each occurrence from the group consisting of CH and CR₅; and T is N.

14. A compound according to Claim 13 wherein R₃ and R₄ are hydrogen; and A is selected from the group consisting of NH, -CH=CH-, and -CH₂NH-.

15. A compound or salt according to Claim 14, wherein R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl) (C₁₋₄ alkyl).

16. A compound according to Claim 14, which is 4-(3-Trifluoromethyl-2-pyridinyl)-N-(3-methoxy-4-hydroxyphenylmethyl)-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

17. A compound according to Claim 14, which is 4-(3-Nitro-2-pyridinyl)-N-[4-(n-butyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

18. A compound according to Claim 14, which is 4-(3-Trifluoromethyl-2-pyridinyl)-N-[4-(n-butyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

19. A compound according to Claim 14, which is 4-(3-Methyl-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

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20. A compound according to Claim 14, which is 4-(3-Methyl-2-pyridinyl)-N-[4-(n-butyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

21. A compound according to Claim 14, which is 4-(3-Chloro-5-trifluoromethyl-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

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22. A compound according to Claim 14, which is 4-(3-Chloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

23. A compound according to Claim 14, which is 4-(3,5-Dichloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

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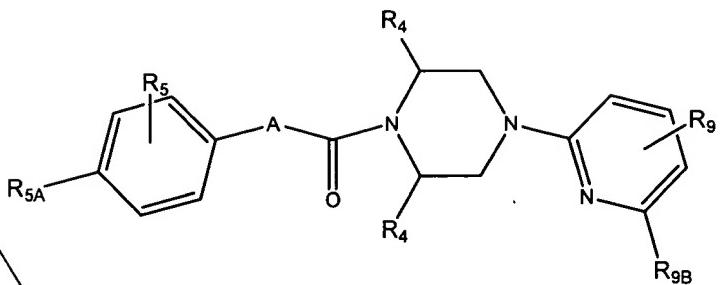
24. A compound according to claim 13, which is 4-(3-Cyano-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide, or a pharmaceutically acceptable salt thereof.

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25. The compound according to claim 13, which is 4-(3-Chloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-2-methyl-1-piperazinecarboxamide.

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26. A compound of the formula:



Sub or a pharmaceutically acceptable salt thereof, wherein:

B4 A is selected from the group consisting of NH, -CH=CH-, and CH₂NH;

R₄ is independently chosen from hydrogen and C₁₋₄ alkyl;

R₅ represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆;

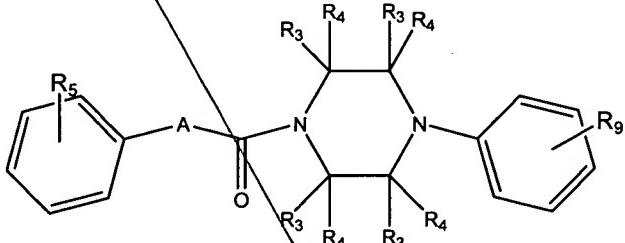
R₉ represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, and -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆;

R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆ alkoxy, -NH(C₁₋₆ alkyl), and -N(C₁₋₆ alkyl)(C₁₋₆ alkyl);

~~R_{9B} is independently selected from the group consisting of halogen, nitro, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆ alkoxy, -NH(C₁₋₆ alkyl), and -N(C₁₋₆ alkyl)(C₁₋₆ alkyl); and~~

~~R₆ is independently selected at each occurrence the group consisting of halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)(C₁₋₄ alkyl).~~

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27. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of a single bond, S, NR_A, CHR_B, NR_ACHR_B, CHR_BNR_A, -CR_A=CR_B-, and C₃H₄; where R_A and R_B are independently selected at each occurrence from the group consisting of hydrogen and alkyl;

R₃ and R₄ are independently selected at each occurrence from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -S(O)_nNHalkyl; optionally substituted -S(O)_nN(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl;

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optionally substituted $-\text{NC}(=\text{O})(\text{alkyl})(\text{alkyl})$; optionally substituted $-\text{NHS(O)alkyl}$; optionally substituted $-\text{NS(O)}_n(\text{alkyl})(\text{alkyl})$; optionally substituted saturated or partially unsaturated heterocycloalkyl of from 5 to 8 atoms, which saturated or partially unsaturated heterocycloalkyl contains 1, 2, or 3 heteroatoms selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring selected from the group consisting of N, O, and S;

or any two

R_3 and R_4 not attached to the same carbon may be joined to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R_5 is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, C_{1-6} alkyl substituted with 0-2 R_6 , C_{2-6} alkenyl substituted with 0-2 R_6 , C_{2-6} alkynyl substituted with 0-2 R_6 , C_{1-6} alkoxy substituted with 0-2 R_6 , $-\text{NH}(\text{C}_{1-6}\text{ alkyl})$ substituted with 0-2 R_6 , $-\text{N}(\text{C}_{1-6}\text{ alkyl})(\text{C}_{1-6}\text{ alkyl})$ where each alkyl is independently substituted with 0-2 R_6 , $-\text{XR}_7$, and Y;

R_9 represents 0-3 substituents and is independently selected at each occurrence from the group consisting of bromo, haloalkyl, haloalkoxy, hydroxy, C_{2-6} alkyl substituted with 0-2 R_6 , C_{2-6} alkenyl substituted with 0-2 R_6 , C_{2-6} alkynyl

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substituted with 0-2 R₆, C₂₋₆ alkoxy substituted with 0-2 R₆, -NH(C₂₋₆ alkyl) substituted with 0-2 R₆, -N(C₂₋₆ alkyl)(C₂₋₆ alkyl) where each C₂₋₆ alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -NH(alkyl), -N(alkyl)(alkyl), -S(O)_n(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl₁)(alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 3 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 3 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), -NHS(O)_n(alkyl), -S(O)_n(alkyl), -S(O)_nNH(alkyl), -S(O)_nN(alkyl₃)(alkyl₄) where alkyl₃ and alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

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~~Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;~~
~~wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and~~

~~n is independently chosen at each occurrence from 0, 1, and 2.~~

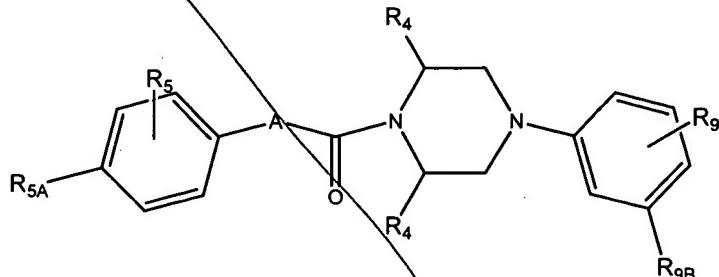
28. A compound or salt according to Claim 27 in which R₃ and R₄ are independently selected at each occurrence from the group consisting of hydrogen and C₁₋₆ alkyl.

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29. A compound or salt according to claim 27, wherein A is selected from the group consisting of NH, -CH=CH-, and CH₂NH; R₃ is hydrogen and R₄ is independently chosen at each occurrence from hydrogen and methyl; and R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)(C₁₋₄ alkyl).

30. A compound of the formula:

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or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH₂NH;

R₄ is independently selected at each occurrence from hydrogen and C₁₋₄alkyl;

R₅ represents 0 to 2 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, and -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆;

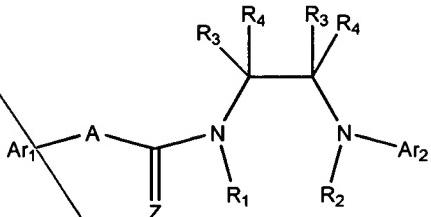
R₉ represents 0 to 2 substituents and is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, and -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆;

R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C₁₋₆ alkyl, C₁₋₆ alkoxy, -NH(C₁₋₆ alkyl), and -N(C₁₋₆ alkyl)(C_{1-C6} alkyl);

R_{9B} is independently selected from the group consisting of trifluoromethoxy, hydroxy, C₂₋₆ alkyl, C₂₋₆ alkoxy, -NH(C₂₋₆ alkyl), and -N(C₂₋₆ alkyl)(C₂₋₆ alkyl); and

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, -NH(C₁₋₄ alkyl), and -N(C₁₋₄ alkyl)(C₁₋₄ alkyl).

31. A compound of the formula:

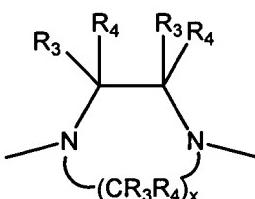


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or a pharmaceutically acceptable salt thereof, wherein the compound or pharmaceutically acceptable salt thereof exhibits an EC₅₀ or K_i of 1 micromolar or less in a standard assay of capsaicin receptor mediated calcium mobilization; and wherein

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-; and C₃H₄; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or C₁₋₆ alkyl;

Z is oxygen or sulfur;

R₁ and R₂ independently represent hydrogen or C₁₋₆ alkyl; or R₁ and R₂ are taken together to form a 5 to 8 membered nitrogen-containing ring of the formula:



wherein x is 1, 2, or 3;

R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆;

~~C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;~~

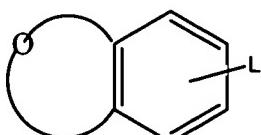
~~or any two~~

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R₃ and R₄ not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar₁ and Ar₂ may be the same or different and are selected from the group consisting of cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R₅; or

Ar₁ and Ar₂ may be the same or different and represent a bicyclic oxygen-containing group of the formula:



optionally mono-, di-, or trisubstituted with R₅, where L represents point of attachment and may be at any point on

the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

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R₅ is independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

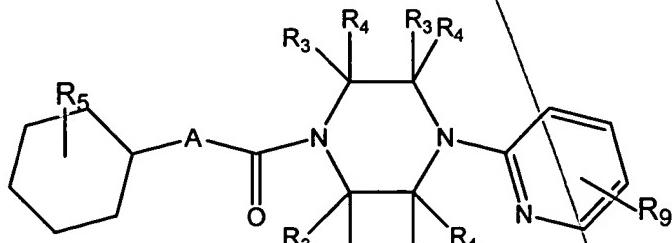
X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n-;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy,

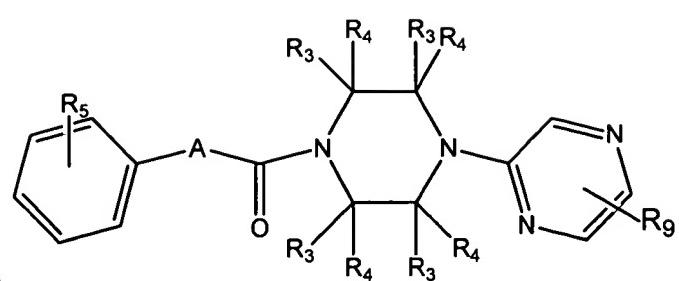
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halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}\text{alkyl})$, $-NH(C_{1-4}\text{alkyl})$, $-N(C_{1-4}\text{alkyl})(C_{1-4}\text{alkyl})$, $-NHC(O)(C_{1-4}\text{alkyl})$, $-N(C_{1-4}\text{alkyl})C(O)(C_{1-4}\text{alkyl})$, $-NHS(O)_n(C_{1-4}\text{alkyl})$, $-S(O)_n(C_{1-4}\text{alkyl})$, $-S(O)_nNH(C_{1-4}\text{alkyl})$, $-S(O)_nN(C_{1-4}\text{alkyl}_3)(C_{1-4}\text{alkyl}_4)$ where $C_{1-4}\text{alkyl}_3$ and $C_{1-4}\text{alkyl}_4$ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y'; Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, $C_{1-4}\text{alkyl}$, $C_{1-4}\text{alkoxy}$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and $C_{1-4}\text{alkylthio}$; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and n is independently chosen at each occurrence from 0, 1, and 2.

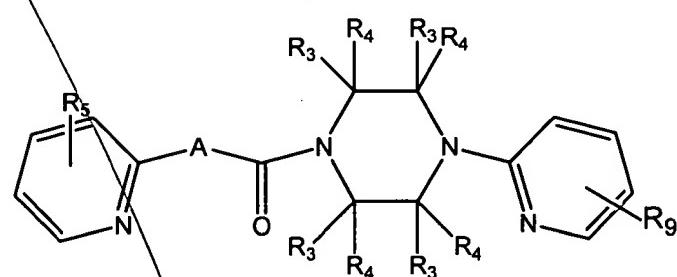
32. A compound of the Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F:



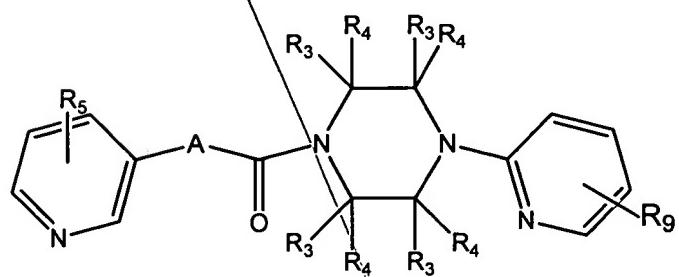
Formula A



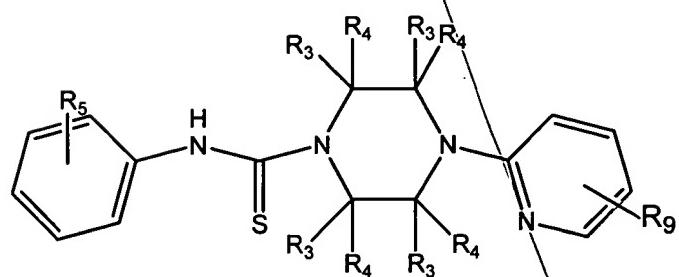
Formula B



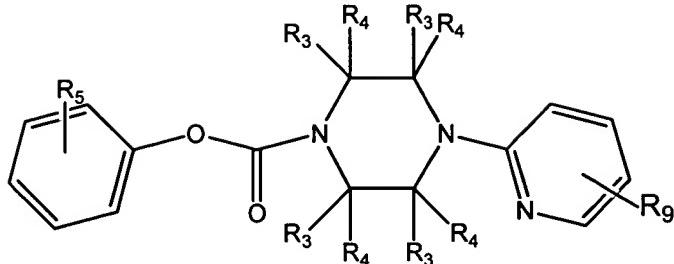
Formula C



Formula D



Formula E



Formula F

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or a pharmaceutically acceptable salt of Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F, wherein A represents NH or O; R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y; or any two R₃ and R₄ not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which

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heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R₅ and R₉ each represent from 1 to 3 substituents and are independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

R₆ is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), -S(O)_n(C₁₋₄alkyl), halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, CO(C₁₋₄alkyl), CONH(C₁₋₄alkyl), CON(C₁₋₄alkyl₁)(C₁₋₄alkyl₂) where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, -XR₇, and Y;

X is independently selected at each occurrence from the group consisting of -CH₂-, -CHR₈-, -O-, -S(O)_n-, -NH-, -NR₈-, -C(=O)-, -C(=O)O-, -C(=O)NH-, -C(=O)NR₈-, -S(O)_nNH-, -S(O)_nNR₈-, NHC(=O)-, -NR₈C(=O)-, -NHS(O)_n-, and -NR₈S(O)_n;

R₇ and R₈ are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C₁₋

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~~C_1-C_4 alkyl, -NH(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NHC(O)(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)C(O)(C_1-C_4 alkyl), -NHS(O)_n(C_1-C_4 alkyl), -S(O)_n(C_1-C_4 alkyl), -S(O)_nNH(C_1-C_4 alkyl), -S(O)_nN(C_1-C_4 alkyl)₃(C_1-C_4 alkyl)₄ where C_1-C_4 alkyl₃ and C_1-C_4 alkyl₄ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y'; Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo(C_1-C_4)alkyl, halo(C_1-C_4)alkoxy, mono- or di(C_1-C_4)alkylamino, and C_1-C_4 alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and n is independently chosen at each occurrence from 0, 1, and 2.~~

33. A compound or salt according to Claim 32, wherein A represents NH.

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34. A compound or salt according to Claim 32, wherein: A represents NH; and R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, hydroxy, amino, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkoxy substituted with 0-2 R₆, -NH(C_1-C_6 alkyl), and -N(C_1-C_6 alkyl)(C_1-C_6 alkyl).

35. A compound or salt according to Claim 32, wherein: A represents NH;

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R₃ represents hydrogen; and

R₄ is independently chosen at each occurrence from hydrogen and C₁₋₆ alkyl.

36. A compound or salt according to Claim 32, wherein:

A represents NH;

R₃ represents hydrogen; and

R₄ is independently chosen at each occurrence from hydrogen and methyl.

37. A compound or salt according to Claim 32, wherein:

A represents NH;

R₃ represents hydrogen;

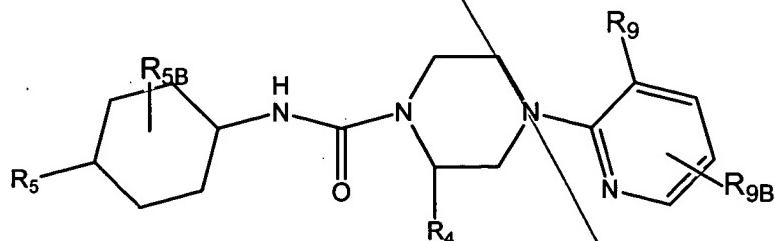
R₄ is independently chosen at each occurrence from hydrogen and methyl; and

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R₅ and R₉ each represent from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈cycloalkyl.

38. A compound or salt according to Claim 37 of the Formula

A-1



Formula A-1

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R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈cycloalkyl; and

R_{5B} and R_{9B} each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3} alkyl, C_{1-3} alkoxy, $-NH(C_{1-3}\text{alkyl})$, and $-N(C_{1-6}\text{alkyl})(C_{1-6}\text{alkyl})$.

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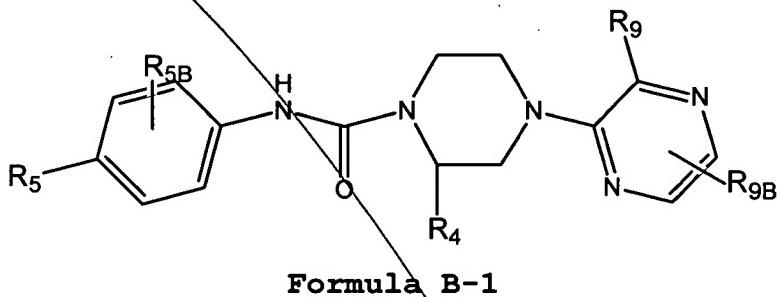
39. A compound or salt according to Claim 38, wherein

R_5 is C_{3-6} alkyl; C_{3-6} alkoxy; halo(C_{1-3})alkyl, halo(C_{1-3})alkoxy, or C_{3-8} cycloalkyl;

R_9 is chloro or trifluoromethyl; and

R_{5B} and R_{9B} are hydrogen.

40. A compound or salt according to Claim 37 of Formula B-
1



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wherein

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-NH(C_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl)(C_{1-6} alkyl), and C_{3-8} cycloalkyl; and

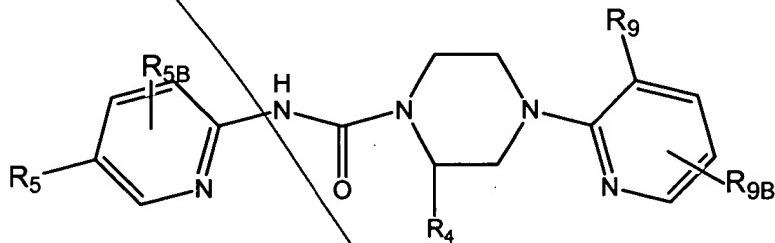
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R_{5B} and R_{9B} each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₃)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

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41. A compound or salt according to Claim 40, wherein:
R₅ is C₃₋₆ alkyl; C₃₋₆ alkoxy; halo(C₁₋₃)alkyl, halo(C₁₋₃)alkoxy, or C₃₋₈ cycloalkyl;
R₉ is chloro or trifluoromethyl; and
R_{5B} and R_{9B} are hydrogen.

42. A compound or salt according to Claim 37 of Formula C-1:



Formula C-1

wherein:

R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈ cycloalkyl; and

R_{5B} and R_{9B} each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino,

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C_{1-3} alkyl, C_{1-3} alkoxy, $-NH(C_{1-3}$ alkyl), and $-N(C_{1-6}$ alkyl) (C_{1-6} alkyl).

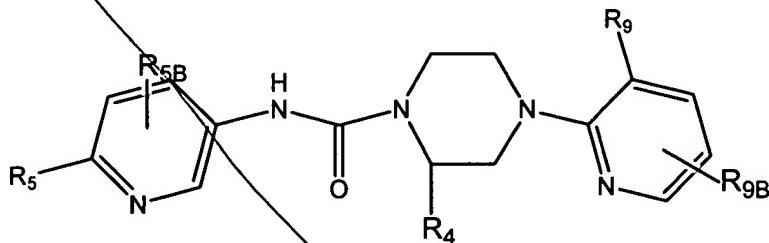
43. A compound or salt according to Claim 42, wherein:

R_5 is C_{3-6} alkyl; C_{3-6} alkoxy; halo(C_{1-3})alkyl, halo(C_{1-3})alkoxy, or C_{3-8} cycloalkyl;

R_9 is chloro or trifluoromethyl; and

R_{5B} and R_{9B} are hydrogen.

44. A compound or salt according to Claim 37 of Formula D-1



Formula D-1

wherein:

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} alkoxy, $-NH(C_{1-6}$ alkyl, $-N(C_{1-6}$ alkyl) (C_{1-6} alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3} alkyl, C_{1-3} alkoxy, $-NH(C_{1-3}$ alkyl), and $-N(C_{1-6}$ alkyl) (C_{1-6} alkyl).

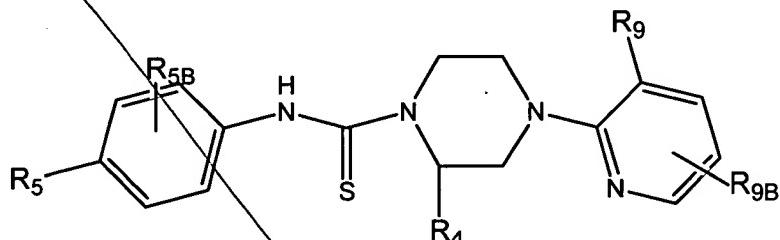
45. A compound or salt according to Claim 44, wherein:

R_5 is C_{3-6} alkyl; C_{3-6} alkoxy; halo(C_{1-3})alkyl, halo(C_{1-3})alkoxy, or C_{3-8} cycloalkyl;

*Sub
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R₉ is chloro or trifluoromethyl; and
R_{5B} and R_{9B} are hydrogen.

46. A compound or salt according to Claim 37, of Formula E-

1



wherein:

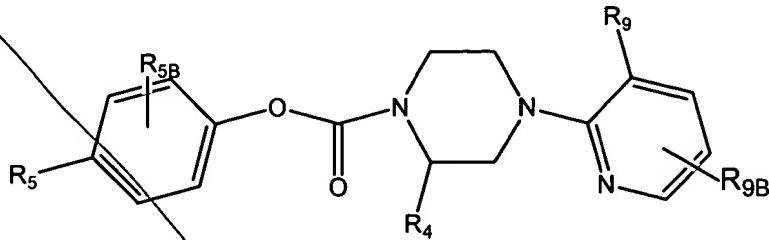
R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈ cycloalkyl; and

R_{5B} and R_{9B} each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

47. A compound or salt according to Claim 46, wherein:

*Sub
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R₅ is C₃₋₆ alkyl; C₃₋₆ alkoxy; halo(C₁₋₃)alkyl, halo(C₁₋₃)alkoxy, or C₃₋₈ cycloalkyl;
R₉ is chloro or trifluoromethyl; and
R_{5B} and R_{9B} are hydrogen.

Suh
48. A compound of salt according to Claim 37 of Formula F-1



Formula F-1

wherein:

R₅ and R₉ are independently selected from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), -N(C₁₋₆alkyl)(C₁₋₆alkyl), and C₃₋₈cycloalkyl; and

R_{5B} and R_{9B} each represent up to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, hydroxy, amino, C₁₋₃alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

Suh
49. A compound or salt according to Claim 47, wherein:

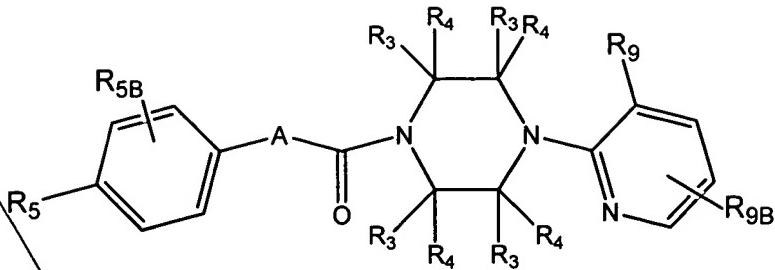
R₅ is C₃₋₆alkyl; C₃₋₆alkoxy; halo(C₁₋₃)alkyl, halo(C₁₋₃)alkoxy, or C₃₋₈cycloalkyl;

R₉ is chloro or trifluoromethyl, and

R_{5B} and R_{9B} are hydrogen.

C1
50. A compound of the Formula:

Suh
B12



Suh
B12

or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or C₁₋₆ alkyl;

R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆; C₂₋₆alkynyl substituted with 0-2 R₆; C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, -XR₇, and Y;

or any two

R₃ and R₄ not attached to the same carbon may be joined to form an aryl ring substituted with 0-3 R₆, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R₆, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R₆ and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

R₅ is selected from the group consisting of bromo, fluoro, iodo, halo(C₁₋₆)alkyl, halo(C₃₋₆)alkoxy, C₃₋₆alkyl substituted with

~~0-3 R₆, C₂₋₆alkenyl substituted with 0-3 R₆, C₂₋₆alkynyl substituted with 0-3 R₆, C₃₋₆alkoxy substituted with 0-2 R₆, (C₃₋₈cycloalkyl)C₁₋₄alkyl, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is substituted with 0-2 R₆, Y, -(C=O)Y, -(CH₂)Y, and -(CH(CN))Y;~~

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B12*
~~R₉ is selected from the group consisting of halogen, cyano, -N(SO₂C₁₋₆alkyl)(SO₂C₁₋₆alkyl), -SO₂NH₂, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, C₁₋₆alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is substituted with 0-2 R₆;~~

~~R_{5B} and R_{9B} each represent from 0 to 2 substituents and are independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl substituted with 0-2 R₆, (C₃₋₈cycloalkyl)C₁₋₄alkyl substituted with 0-2 R₆, C₂₋₆alkenyl substituted with 0-2 R₆, C₂₋₆alkynyl substituted with 0-2 R₆, C₁₋₆alkoxy substituted with 0-2 R₆, -NH(C₁₋₆alkyl) substituted with 0-2 R₆, and -N(C₁₋₆alkyl)(C₁₋₆alkyl) where each C₁₋₆alkyl is independently substituted with 0-2 R₆, and Y; and any two~~

~~R₅ and R_{5B} bound to adjacent atoms may be joined to form a C₃₋₈cycloalkyl group or a heterocycloalkyl group, each of which is optionally substituted by from 1 to 5 substituents independently chosen from cyano, halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), -N(C₁₋₄alkyl)(C₁₋₄alkyl), halo(C₁₋₄)alkyl, and halo(C₁₋₄)alkoxy, wherein the heterocycloalkyl group consists of from 4 to 8 atoms and contains 1, 2, or 3 heteroatoms selected from N, O, and S;~~

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Bl²

R_6 is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C_{1-4} alkyl, C_{1-4} alkoxy, $-NH(C_{1-4}\text{alkyl})$, $-N(C_{1-4}\text{alkyl})(C_{1-4}\text{alkyl})$, $-S(O)_n(C_{1-4}\text{alkyl})$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}\text{alkyl})$, $CONH(C_{1-4}\text{alkyl})$, $CON(C_{1-4}\text{alkyl}_1)(C_{1-4}\text{alkyl}_2)$ where alkyl₁ and alkyl₂ may be joined to form a heterocycloalkyl ring of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}\text{alkyl})$, $-NH(C_{1-4}\text{alkyl})$, $-N(C_{1-4}\text{alkyl})(C_{1-4}\text{alkyl})$, $-NHC(O)(C_{1-4}\text{alkyl})$, $-N(C_{1-4}\text{alkyl})C(O)(C_{1-4}\text{alkyl})$, $-NHS(O)_n(C_{1-4}\text{alkyl})$, $-S(O)_n(C_{1-4}\text{alkyl})$, $-S(O)_nNH(C_{1-4}\text{alkyl})$, $-S(O)_nN(C_{1-4}\text{alkyl}_3)(C_{1-4}\text{alkyl}_4)$ where $C_{1-4}\text{alkyl}_3$ and $C_{1-4}\text{alkyl}_4$ may be joined to form a heterocycloalkyl ring consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently

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b12

selected from halogen, oxo, hydroxy, amino, nitro, cyano, C₁₋₄alkyl, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, mono- or di(C₁₋₄)alkylamino, and C₁₋₄alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

51. A compound or salt according to Claim 50, wherein:
A is O or NR_A, wherein R_A is hydrogen or methyl.

Sub C

52. A compound or salt according to Claim 50, wherein:
A is O or NR_A, wherein R_A is hydrogen or methyl; and
R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

53. A compound or salt according to Claim 50, wherein:
A is O or NR_A, wherein R_A is hydrogen or methyl;
R₃ is hydrogen; and
R₄ is independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl).

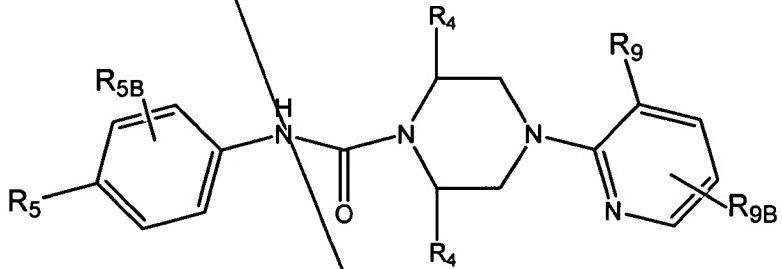
54. A compound or salt according to Claim 50, wherein:
A is O or NR_A, wherein R_A is hydrogen or methyl;
R₃ is hydrogen; and

R₄ is independently chosen at each occurrence from hydrogen and C₁₋₆alkyl.

55. A compound or salt according to Claim 50, wherein:
A is NR_A, wherein R_A is hydrogen or methyl;
R₃ is hydrogen; and
R₄ is independently chosen at each occurrence from hydrogen, halo(C₁₋₃)alkyl, and C₁₋₆alkyl.

56. A compound or salt according to Claim 50, wherein:
A is NR_A, wherein R_A is hydrogen or methyl;
R₃ is hydrogen; and
R₄ is independently chosen at each occurrence from hydrogen and C₁₋₄alkyl.

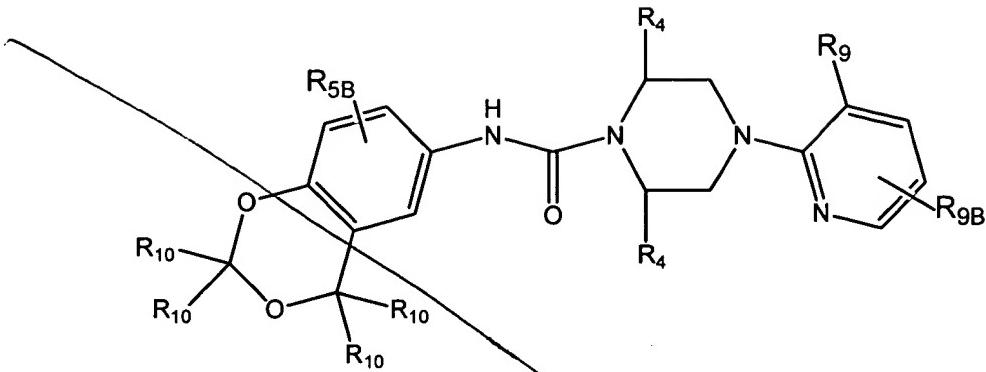
57. A compound or salt according to Claim 50 of the Formula



wherein:

R₄ is independently chosen at each occurrence from hydrogen and C₁₋₄alkyl.

58. A compound or salt according to Claim 57 of the formula:



wherein

R_{5B} and R_{9B} are independently chosen from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and

R₁₀ is independently chosen at each occurrence from hydrogen, halogen, and C₁₋₄ alkyl.

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59. A compound or salt according to Claim 58 wherein:

R₉ is selected from the group consisting of halogen, cyano, -N(SO₂CH₃)₂, -SO₂NH₂, halo(C₁₋₃)alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₃alkyl)(C₁₋₃alkyl).

60. A compound or salt according to Claim 57, wherein:

R_{5B} and R_{9B} are independently chosen from hydrogen, halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy.

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61. A compound or salt according to Claim 57, wherein:

R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and

R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, and C₁₋₂alkyl, and C₁₋₂alkoxy.

62. A compound or salt according to Claim 57, wherein:

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~~R₉ is selected from the group consisting of halogen, cyano, -N(SO₂CH₃)₂, -SO₂NH₂, halo(C₁₋₃)alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₃alkyl)(C₁₋₃alkyl);~~

~~R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and~~

~~R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, and C₁₋₂alkyl, and C₁₋₂alkoxy.~~

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B14
63. A compound or salt according to Claim 57, wherein:

~~R₅ is selected from the group consisting of bromo, fluoro, iodo, halo(C₁₋₆)alkyl, halo(C₃₋₆)alkoxy, C₃₋₆alkyl substituted with 0-3 R₆, C₂₋₆alkenyl substituted with 0-3 R₆, Y, -(C=O)Y, -(CH₂)Y, and -(CH(CN))Y;~~

~~R₉ is selected from the group consisting of halogen, cyano, -N(SO₂CH₃)₂, -SO₂NH₂, halo(C₁₋₂)alkyl, C₁₋₃alkoxy, -NH(C₁₋₆alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl);~~

~~R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and~~

~~R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, and C₁₋₂alkyl, and C₁₋₂alkoxy.~~

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(1)
64. A compound or salt according to Claim 63, wherein:

~~R₆ is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C₁₋₄alkyl, C₁₋₄alkoxy, -NH(C₁₋₄alkyl), and -N(C₁₋₄alkyl)(C₁₋₄alkyl) and Y; and~~

~~Y is independently selected at each occurrence from C₃₋₈ cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with~~

one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, -cyano, C₁₋₄alkyl, C₁₋₄alkoxy, halo(C₁₋₄)alkyl, halo(C₁₋₄)alkoxy, mono- or di(C₁₋₄)alkylamino, and C₁₋₄alkylthio.

65. A compound or salt according to Claim 63, wherein:

R₉ is cyano, trifluoromethyl, chloro, or iodo; and

R_{9B} is hydrogen.

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Cl 66. A compound according to Claim 50, which is

N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

67. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-cyclohexylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

68. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

69. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

70. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

71. A compound according to Claim 50, which is (2S)-4-(3-chloropyridin-2-yl)-N-(4-trifluoromethylphenyl)-2-

methyl

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piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

72. A compound according to Claim 50, which is (2S)-N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

73. A compound according to Claim 50, which is (2S)-4-(3-chloropyridin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

74. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-(4-piperidin-1-ylphenyl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

75. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[2-fluoro-4-(trifluoromethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

76. A compound according to Claim 50, which is (2R)-2-methyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

77. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

78. A compound according to Claim 50, which is (2R)-N-(4-isopropylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-

yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

79. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-2,6-dimethyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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80. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2,6-dimethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

81. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-N-(4-isopropylphenyl)-2,6-dimethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

82. A compound according to Claim 50, which is (2R)-N-(4-cyclohexylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

83. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-N-(4-cyclohexylphenyl)-2,6-dimethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

84. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-cyclopentylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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Cl*

85. A compound according to Claim 50, which is (2R)-N-(4-cyclopentylphenyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

86. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-[3-(dimethylamino)pyridin-2-yl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

87. A compound according to Claim 50, which is (2R)-4-[3-(dimethylamino)pyridin-2-yl]-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

88. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-methoxypyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

*Sub
Cl*

89. A compound according to Claim 50, which is (2R)-4-(3-methoxypyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

90. A compound according to Claim 50, which is (2R)-N-(4-cyclohexylphenyl)-4-(3-methoxypyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

91. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(3,6-dihydro-2H-pyran-4-yl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

*Sub
cl*

92. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-(4-tetrahydro-2H-pyran-4-ylphenyl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

93. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(4-hydroxytetrahydro-2H-pyran-4-yl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

94. A compound according to Claim 50, which is (2R)-N-[4-(4-hydroxytetrahydro-2H-pyran-4-yl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

95. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-(2-methyl-1,3-thiazol-4-yl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

96. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(2-ethyl-1,3-thiazol-4-yl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

97. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(2-methoxy-1,1-dimethylethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

Sub C1

98. A compound according to Claim 50, which is (2R)-N-[4-(2-methoxy-1,1-dimethylethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

99. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-(1-cyano-1-methylethyl)phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

100. A compound according to Claim 50, which is (2R)-N-[4-(1-cyano-1-methylethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

101. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-ethylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

102. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-2-ethyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

103. A compound according to Claim 50, which is 4-(3-chloropyridin-2-yl)-2-ethyl-N-(4-isopropylphenyl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

104. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-2-ethyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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105. A compound according to Claim 50, which is 2-ethyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

106. A compound according to Claim 50, which is 2-ethyl-N-(4-isopropylphenyl)-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

107. A compound according to Claim 50, which is 2-tert-butyl-N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

108. A compound according to Claim 50, which is 2-tert-butyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

109. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)-2-isopropylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

110. A compound according to Claim 50, which is N-(4-tert-butylphenyl)-2-isopropyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

111. A compound according to Claim 50, which is 2-isopropyl-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)

~~pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~112. A compound according to Claim 50, which is 2-isopropyl-N-(4-isopropylphenyl)-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

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~~113. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~114. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~115. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~116. A compound according to Claim 50, which is (2R)-N-(4-cyclohexylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~117. A compound according to Claim 50, which is (2R)-N-(4-cyclopentylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~118. A compound according to Claim 50, which is (2R)-N-(4-tert-butylphenyl)-4-(3-cyanopyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

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119. A compound according to Claim 50, which is (2R)-4-(3-cyanopyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

120. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-[cyano(phenyl)methyl] phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

121. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[3-methyl-4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

122. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[3-methyl-4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

123. A compound according to Claim 50, which is (2R)-4-[3-[bis(methylsulfonyl)amino]pyridin-2-yl]-N-(4-tert-butylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

124. A compound according to Claim 50, which is (2R)-2-methyl-N-[3-methyl-4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl] piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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125. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-[1-(trifluoromethyl)vinyl]phenyl] piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

126. A compound according to Claim 50, which is (2R)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]-N-[4-[1-(trifluoromethyl)vinyl] phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

127. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[4-[1-(trifluoromethyl)vinyl] phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

128. A compound according to Claim 50, which is (2R)-N-(4-sec-butylphenyl)-4-(3-fluoropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

129. A compound according to Claim 50, which is (2R)-2-methyl-N-[4-(2,2,2-trifluoro-1-methylethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

130. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-[4-(2,2,2-trifluoro-1-methylethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

131. A compound according to Claim 50, which is (2R)-4-(3-chloro-5-nitropyridin-2-yl)-2-methyl-N-[4-

(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

132. A compound according to Claim 50, which is (2R)-4-(5-amino-3-chloropyridin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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133. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-N-[3-fluoro-4-(trifluoromethyl) phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

134. A compound according to Claim 50, which is (2R)-N-[3-fluoro-4-(trifluoromethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl) pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

135. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[4-(2,2,2-trifluoro-1-methylethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

136. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

137. A compound according to Claim 50, which is (2R)-4-(3-fluoropyridin-2-yl)-2-methyl-N-(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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138. A compound according to Claim 50, which is (2R)-2-methyl-N-(2,2,4,4-tetrafluoro-4H-1,3-benzodioxin-6-yl)-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

139. A compound according to Claim 50, which is (2R)-4-[3-(aminosulfonyl)pyridin-2-yl]-N-(4-tert-butylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

140. A compound according to Claim 50, which is (2R)-N-(4-benzoylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

141. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-iodophenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

142. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-{4-[2,2,2-trifluoro-1,1-bis(trifluoromethyl)ethyl]phenyl}piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

143. A compound according to Claim 50, which is (2R)-2-methyl-N-{4-[2,2,2-trifluoro-1,1-bis(trifluoromethyl)ethyl]phenyl}-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

144. A compound according to Claim 50, which is (2R)-N-(4-butylphenyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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~~145. A compound according to Claim 50, which is 2-(fluoromethyl)-N-[4-(trifluoromethyl)phenyl]-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~146. A compound according to Claim 50, which is (2R)-N-[4-bromo-3-(trifluoromethyl)phenyl]-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~147. A compound according to Claim 50, which is (2R)-N-[4-bromo-3-(trifluoromethyl)phenyl]-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~148. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-N-[4-fluoro-3-(trifluoromethyl) phenyl]-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~149. A compound according to Claim 50, which is (2R)-N-[4-fluoro-3-(trifluoromethyl) phenyl]-2-methyl-4-[3-(trifluoromethyl) pyridin-2-yl] piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~150. A compound according to Claim 50, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-{4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl] phenyl}piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.~~

~~151. A compound according to Claim 50, which is (2R)-2-methyl-N-{4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)~~

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ethyl]phenyl}-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

152. A compound according to Claim 40, which is (2R)-N-(4-tert-butylphenyl)-4-(3-chloropyrazin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

153. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-N-(4-isopropylphenyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

154. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

155. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-{4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethyl] phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

156. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-{4-cyclopentyl-phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

157. A compound according to Claim 40, which is (2R)-4-(3-chloropyrazin-2-yl)-2-methyl-N-{4-cyclohexyl-phenyl} piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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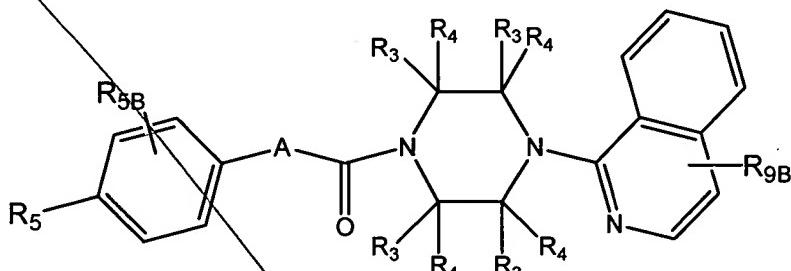
158. A compound according to Claim 42, which is 4-(3-chloropyridin-2-yl)-N-[5-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

159. A compound according to Claim 42, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[5-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

160. A compound according to Claim 42, which is (2R)-4-(3-chloropyridin-2-yl)-2-methyl-N-[6-(trifluoromethyl)pyridin-3-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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161. A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B- , and C₃H₄; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or C₁₋₆ alkyl;

R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl,

~~C₂-6alkenyl, C₂-6alkynyl, C₁-6alkoxy, -NH(C₁-6alkyl), and
-N(C₁-6alkyl)(C₁-6alkyl);~~

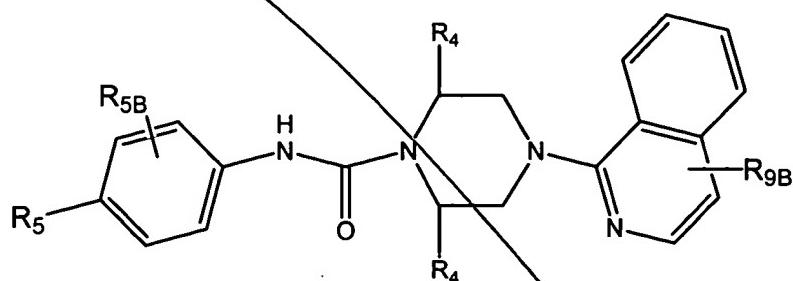
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~~R₅ is selected from the group consisting of halogen, halo(C₁-₆)alkyl, C₃-6alkyl substituted with 0-3 R₆, C₂-6alkenyl substituted with 0-3 R₆, (C₃-8cycloalkyl)C₁-4alkyl substituted with 0-3 R₆, and Y;~~

~~R_{5B} and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C₁-2)alkyl, halo(C₁-2)alkoxy, amino, C₁-4alkyl, and C₁-2alkoxy;~~

~~R₆ is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C₁-4alkyl, C₁-4alkoxy, -NH(C₁-4alkyl), and -N(C₁-4alkyl)(C₁-4alkyl) and Y;~~

~~Y is independently selected at each occurrence from C₃-8 cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C₁-4alkyl, C₁-4alkoxy, halo(C₁-4)alkyl, halo(C₁-4)alkoxy, mono- or di(C₁-4)alkylamino, and C₁-4alkylthio.~~

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162. A compound or salt according to Claim 161 of the
Formula:



wherein

R₄ is independently selected at each occurrence from hydrogen and C₁₋₄alkyl.

163. A compound or salt according to Claim 162, wherein:

R₅ is selected from the group consisting of halo(C₁₋₆)alkyl, C₃₋₆alkyl, (C₃₋₈cycloalkyl)C₁₋₄alkyl, and Y;

R_{5B} and R_{9B} each represent from 0 to 1 substituents and are independently chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy;

Y is selected from C₃₋₈ cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl.

164. A compound according to Claim 161, which is (2R)-4-isoquinolin-1-yl-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

165. A compound according to Claim 161, which is (2R)-N-(4-tert-butylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

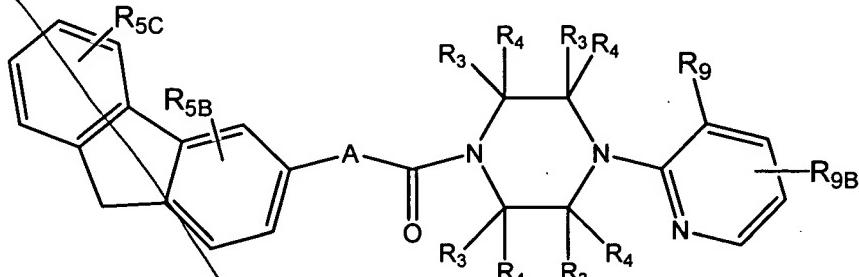
166. A compound according to Claim 161, which is (2R)-N-(4-isopropylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

167. A compound according to Claim 161, which is (2R)-N-(4-cyclopentylphenyl)-4-isoquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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168. A compound according to Claim 161, which is (2R)-N-(4-cyclohexylphenyl)-4-isquinolin-1-yl-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

169. A compound of the Formula:



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or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_{B'}, NR_ACR_BR_{B'}, CR_BR_{B'}NR_A, -CR_A=CR_B-; where R_A, R_B, and R_{B'} are independently selected at each occurrence from hydrogen or C₁₋₆ alkyl;

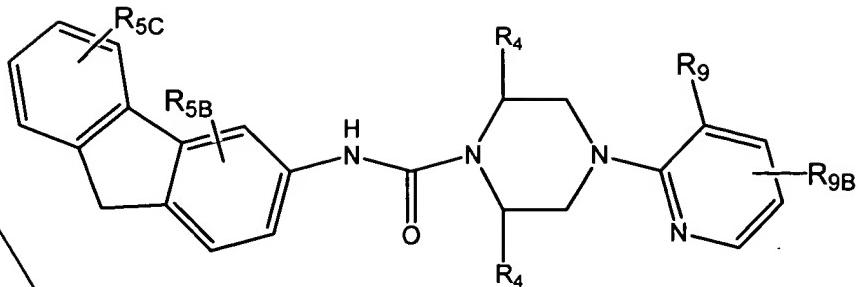
R₃ and R₄ are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C₁₋₆)alkyl, halo(C₁₋₆)alkoxy, hydroxy, amino, C₁₋₆alkyl, C₂₋₆alkenyl, C₂₋₆alkynyl, C₁₋₆alkoxy, -NH(C₁₋₆alkyl), and -N(C₁₋₆alkyl)(C₁₋₆alkyl);

R_{5B}, R_{5C}, and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and

R₉ is selected from the group consisting of halogen, cyano, -N(SO₂CH₃)₂, -SO₂NH₂, halo(C₁₋₃)alkyl, C₁₋₃alkoxy, -NH(C₁₋₃alkyl), and -N(C₁₋₃alkyl)(C₁₋₃alkyl)

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170. A compound or salt according to Claim 169 of the Formula:



wherein

R₄ is independently selected at each occurrence from hydrogen and C₁₋₄alkyl.

171. A compound or salt according to Claim 170, wherein:

R₉ is selected from the group consisting of halogen and halo(C₁₋₂)alkyl; and

R_{5B} and R_{9B} each represent from 0 to 1 substituents and are independently chosen from halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy.

172. A compound according to Claim 169, which is (2R)-4-(3-chloropyridin-2-yl)-N-(9H-fluoren-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

173. A compound according to Claim 169, which is (2R)-N-(9H-fluoren-2-yl)-2-methyl-4-[3-(trifluoromethyl) pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

174. A compound according to Claim 38, which is (2R)-N-(4-tert-butylcyclohexyl)-4-(3-chloropyridin-2-yl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

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175. A compound according to Claim 38, which is (2R)-4-(3-chloropyridin-2-yl)-N-(4-isopropylcyclohexyl)-2-methylpiperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

176. A compound according to Claim 38, which is (2R)-N-(4-isopropylcyclohexyl)-2-methyl-4-[3-(trifluoromethyl)pyridin-2-yl]piperazine-1-carboxamide, or a pharmaceutically acceptable salt thereof.

177. A method of reducing the calcium conductance of a capsaicin receptor, which method comprises: contacting a first solution comprising a fixed concentration of a capsaicin receptor agonist and a compound or salt of Claim 50 with a cell expressing the capsaicin receptor, wherein the compound or salt is present in the solution at a concentration sufficient to produce a detectable reduction of the calcium mobilization effects of the capsaicin receptor agonist when tested in an *in vitro* assay in which cells expressing a capsaicin receptor are contacted with a second solution comprising the fixed concentration of capsaicin receptor agonist and the compound or salt.

178. The method of Claim 177 wherein the cell expressing the capsaicin receptor is a neuronal cell that is contacted *in vivo* in an animal, and wherein the first solution is a body fluid of said animal.

179. The method of Claim 177 wherein the animal is a human patient.

180. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt of Claim 50.

181. A package comprising a pharmaceutical composition of claim 180 in a container and further comprising indicia comprising instructions for using the composition to alleviate pain.

182. A package comprising a pharmaceutical composition of claim 180 in a container and further comprising indicia comprising instructions for using the composition to treat a patient suffering from urinary incontinence.

183. A package comprising a pharmaceutical composition of claim 180 in a container and further comprising indicia comprising instructions for using the composition to alleviate symptoms of exposure to capsaicin or tear gas.

184. A compound or salt of Claim 50 wherein, in an in vitro assay of capsaicin receptor antagonism, the compound or salt exhibits capsaicin receptor antagonist activity, but in an in vitro assay of capsaicin receptor agonism the compound does not exhibit detectable agonist activity.

185. A compound or salt of Claim 50 wherein a dose of the compound or salt that is twice the minimum dose sufficient to provide analgesia in an animal model for determining pain relief does not produce sedation in an animal model assay of sedation.

186. A method of treating a mammal suffering from at least one symptom selected from the group consisting of symptoms of

exposure to capsaicin, symptoms of burns or irritation due to exposure to heat, symptoms of burns or irritation due to exposure to light, symptoms of burns, bronchoconstriction or irritation due to exposure to tear gas, and symptoms of burns or irritation due to exposure to acid, the method comprising administering to the mammal a therapeutic dose of a compound that is a high potency capsaicin receptor antagonist in an *in vitro* assay of capsaicin receptor antagonism, is not a capsaicin analog; wherein the therapeutic dose contains an amount of the compound that is effective to reduce severity of at least one of said at least one symptom.

187. The method of claim 186 wherein the compound is a compound or salt of any of claims 1-176.

188. A method of treating a mammal suffering from neuropathic pain, the method comprising administering to the mammal a therapeutically effective amount of a compound that is a high potency capsaicin receptor antagonist in an *in vitro* assay of capsaicin receptor antagonism.

189. A method of treating a mammal suffering from peripheral-nerve-mediated pain, the method comprising administering to the mammal a therapeutic dose of a compound that is a capsaicin receptor antagonist, wherein the compound is a high potency capsaicin receptor antagonist in an *in vitro* assay of capsaicin receptor antagonism and is not a capsaicin analog,

wherein the therapeutic dose contains an amount of the compound that is effective to reduce the peripheral-nerve-mediated pain.

190. The method of Claim 189 wherein the compound is a compound or salt of Claim 50.

191. The method of claim 189 wherein the pain is neuropathic pain.

192. The method of Claim 190 wherein the pain is associated with a condition selected from the group consisting of postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, Charcot's pain, toothache, venomous snake bite, spider bite, insect sting, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, sciatic neuritis, peripheral neuritis, polyneuritis, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis, Gombault's neuritis, neuronitis, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngial neuralgia, migranous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, mandibular joint neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, vidian neuralgia, sinus headache, tension headache, labor, childbirth, intestinal gas, menstruation, cancer, and trauma.

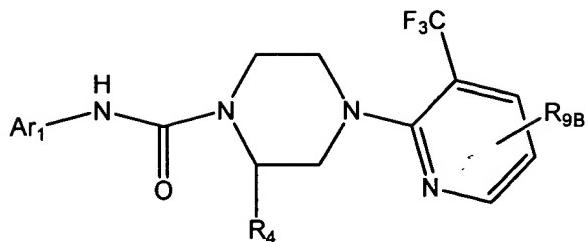
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C1 193. A compound or salt of Claim 50 wherein the compound or salt is not addictive.

194. The use of a compound according to Claim 1, 4, 9, 31, or 50 for the manufacture of a medicament for the treatment of pain.

195. The use of a compound according to Claim 1, 4, 9, 31, or 50 for the manufacture of a medicament for the treatment of neuropathic pain.

196. The use of a compound according to Claim 1, 4, 9, 31, or 50 for the manufacture of a medicament for the treatment of the pain associated with a condition selected from the group consisting of postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, charcot's pain, toothache, venomous snake bite, spider bite, insect sting, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, sciatic neuritis, peripheral neuritis, polyneuritis, optic neuritis, postfebrile neuritis, migrating neuritis, segmental neuritis, Gombault's neuritis, neuronitis, cervicobrachial neuralgia, cranial neuralgia, geniculate neuralgia, glossopharyngial neuralgia, migranous neuralgia, idiopathic neuralgia, intercostals neuralgia, mammary neuralgia, mandibular joint neuralgia, Morton's neuralgia, nasociliary neuralgia, occipital neuralgia, red neuralgia, Sluder's neuralgia, splenopalatine neuralgia, supraorbital neuralgia, vidian neuralgia, sinus headache, tension headache, labor, childbirth, intestinal gas, menstruation, cancer, and trauma.

Scb
C1
197. A compound of the Formula



or a pharmaceutically acceptable salt thereof wherein:

*SUB
Cl*

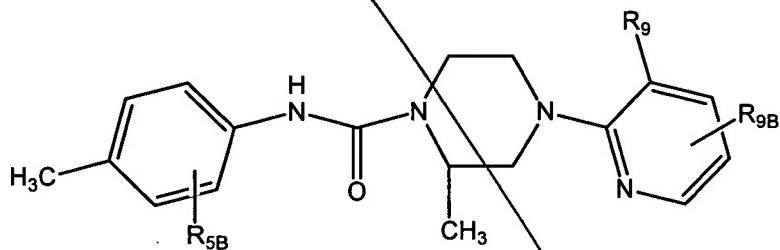
R₄ is methyl or hydrogen;

R_{9B} represents 0-2 substituents independently chosen from:

halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy,
amino, C₁₋₄alkyl, and C₁₋₂alkoxy; and

Ar₁ is 2,4-dichlorophenyl or 3-nitro-4-chlorophenyl.

198. A compound of the Formula



or a pharmaceutically acceptable salt thereof wherein:

R₉ is chloro or trifluoromethyl; and

R_{5B} and R_{9B} independently represent from 0-2 substituents on each of the rings on which they occur and are independently chosen from: halogen, cyano, nitro, halo(C₁₋₂)alkyl, halo(C₁₋₂)alkoxy, amino, C₁₋₄alkyl, and C₁₋₂alkoxy.

*add
B17*